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Moodie, Shonna
Waters, Steve
Wong, Chi-Wai
Metabolex, Inc.

<120> Methods of Diagnosing & Treating Diabetes and Insulin
Resistance

<130> 016325-013800PC

<140> WO PCT/US03/17941

<141> 2003-06-04

<150> US 60/385,996

<151> 2002-06-04

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Gly Phe Leu Gly Asn Ser Val Ala Ile Trp Met Phe Val Phe His Met
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Lys Pro Trp Ser Gly Ile Ser Val Tyr Met Phe Asn Leu Ala Leu Ala
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Asp Phe Leu Tyr Val Leu Thr Leu Pro Ala Leu Ile Phe Tyr Tyr Phe
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Asn Lys Thr Asp Trp Ile Phe Gly Asp Ala Met Cys Lys Leu Gln Arg
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Phe Ile Phe His Val Asn Leu Tyr Gly Ser Ile Leu Phe Leu Thr Cys
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 precursor, cysteine-rich motorneuron 1 (CRIM1)
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ctacagcact	gtgcagaaca	agcattccca	cttggcctca	agataactga	ccacatgttt	3300

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<210> 14

<211> 1028

<212> PRT

<213> Mus musculus

<220>

<223> mouse cysteine-rich repeat-containing protein,
cysteine-rich motorneuron 1 (CRIM1), partial

<400> 14

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 1             5             10             15

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Leu Leu Ala Arg Ser Gly Thr Arg Ala Leu Val Cys Leu Pro Cys Asp
      20             25             30

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```

Glu Ser Lys Cys Glu Glu Pro Arg Ser Cys Pro Gly Ser Ile Val Gln
      35             40             45

```

```

Gly Val Cys Gly Cys Cys Tyr Met Cys Ala Arg Gln Arg Asn Glu Ser
      50             55             60

```

```

Cys Gly Gly Ala Tyr Gly Leu His Gly Ala Cys Asp Arg Gly Leu Arg
      65             70             75             80

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```

Cys Val Ile Arg Pro Pro Leu Asn Gly Asp Ser Ile Thr Glu Tyr Glu
      85             90             95

```

```

Val Gly Val Cys Glu Asp Glu Asp Trp Asp Asp Asp Gln Leu Ile Gly
      100            105            110

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```

Phe Glu Pro Cys Asn Glu Asn Leu Ile Ser Gly Cys Asn Ile Ile Asn
      115            120            125

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Gly Lys Cys Glu Cys Gly Thr Ile Arg Thr Cys Asn Asn Pro Phe Glu
      130            135            140

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Phe Pro Arg Lys Asp Met Cys Leu Ser Ala Leu Lys Arg Ile Glu Glu
      145            150            155            160

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Glu Lys Pro Asp Cys Ser Lys Ala Arg Cys Glu Val Arg Phe Ser Pro
      165            170            175

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Arg Cys Pro Glu Asp Ser Ile Leu Ile Glu Gly Tyr Ala Pro Pro Gly
      180            185            190

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Glu Cys Cys Pro Leu Pro Ser Arg Cys Val Cys Asp Pro Gly Cys
 195 200 205

Leu Arg Lys Val Cys Gln Pro Gly Tyr Leu Asn Ile Leu Val Ser Lys
 210 215 220

Ala Ser Gly Lys Pro Gly Glu Cys Cys Asp Leu Tyr Glu Cys Lys Pro
 225 230 235 240

Val Phe Ser Val Asp Cys Ser Thr Val Glu Cys Pro Pro Val Gln Gln
 245 250 255

Ala Val Cys Pro Leu Asp Ser Tyr Glu Thr Gln Val Arg Leu Thr Ala
 260 265 270

Asp Gly Cys Cys Thr Leu Pro Ala Arg Cys Glu Cys Leu Ser Gly Leu
 275 280 285

Cys Gly Phe Pro Val Cys Glu Val Gly Ser Thr Pro Arg Ile Val Ser
 290 295 300

Arg Gly Asp Gly Thr Pro Gly Lys Cys Cys Asp Val Phe Glu Cys Val
 305 310 315 320

Asn Glu Thr Lys Pro Ala Cys Val Phe Asn Ser Val Glu Tyr Tyr Asp
 325 330 335

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 340 345 350

Gly Val Ser Ile Cys Phe Thr Ala Gln Cys Gly Glu Leu Asn Cys Glu
 355 360 365

Arg Tyr Tyr Val Pro Glu Gly Glu Cys Cys Pro Val Cys Glu Asp Pro
 370 375 380

Ile Tyr Pro Leu Asn Asn Pro Ala Gly Cys Tyr Ala Asn Gly Gln Ile
 385 390 395 400

Arg Ala His Gly Asp Arg Trp Arg Glu Asp Asp Cys Thr Phe Cys Gln
 405 410 415

Cys Ile Asn Gly Glu Pro His Cys Val Ala Thr Ala Cys Gly Gln Ser
 420 425 430

Cys Met His Pro Val Lys Val Pro Gly Glu Cys Cys Pro Val Cys Glu
 435 440 445

Glu Pro Thr Tyr Ile Thr Ile Asp Pro Pro Ala Cys Gly Glu Leu Ser
 450 455 460

Asn Cys Ser Leu Lys Glu Lys Asp Cys Val Tyr Gly Phe Lys Leu Asp
 465 470 475 480

His Asn Gly Cys Arg Thr Cys Gln Cys Lys Ile Arg Glu Glu Leu Cys
 485 490 495

Leu Gly Leu Lys Arg Ala Cys Thr Leu Asp Cys Pro Phe Gly Phe Leu
 500 505 510

Thr Asp Val His [REDACTED] Cys Glu Leu Cys Gln Cys Arg Pro [REDACTED] Pro Lys
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 Lys Cys Arg Pro Thr Met Cys Asp Lys Phe Cys Pro Leu Gly Phe Leu
 530 535 540
 Lys Asn Lys His Gly Cys Asp Ile Cys Arg Cys Lys Lys Cys Pro Glu
 545 550 555 560
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 565 570 575
 Gly Cys Leu Ile Cys Lys Cys Arg Glu Val Pro Pro Ser Ala Gly Pro
 580 585 590
 Pro Val Leu Ser Gly Thr Cys Leu Ser Met Asp Gly His His His Lys
 595 600 605
 Asn Glu Glu Ser Trp His Asp Gly Cys Arg Glu Cys Tyr Cys His Asn
 610 615 620
 Gly Lys Glu Met Cys Ala Leu Ile Thr Cys Pro Val Pro Ala Cys Gly
 625 630 635 640
 Asn Pro Thr Ile Arg Ser Gly Gln Cys Cys Pro Ser Cys Thr Asp Asp
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 Phe Val Val Gln Lys Pro Glu Leu Ser Thr Pro Ser Ile Cys His Ala
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 Pro Gly Gly Glu Tyr Phe Val Glu Gly Glu Thr Trp Asn Ile Asp Ser
 675 680 685
 Cys Thr Gln Cys Thr Cys His Ser Gly Arg Val Leu Cys Glu Thr Glu
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 Val Cys Pro Pro Leu Leu Cys Gln Asn Pro Ser Arg Thr Gln Asp Ser
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 Cys Cys Pro Gln Cys Thr Asp Asp Pro Pro Gln Pro Ser Thr Ser His
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 Asn Glu Ser Val Pro Ser Tyr Cys Arg Asn Asp Glu Gly Asp Ile Phe
 740 745 750
 Leu Ala Ala Glu Ser Trp Lys Pro Asp Ala Cys Thr Ser Cys Val Cys
 755 760 765
 Val Asp Ser Ala Ile Ser Cys Tyr Ser Glu Ser Cys Pro Ser Val Ala
 770 775 780
 Cys Glu Arg Pro Val Leu Arg Lys Gly Gln Cys Cys Pro Tyr Cys Leu
 785 790 795 800
 Glu Asp Thr Ile Pro Lys Lys Val Val Cys His Phe Ser Gly Lys Thr
 805 810 815
 Tyr Ala Asp Glu Glu Arg Trp Asp Ile Asp Ser Cys Thr His Cys Tyr
 820 825 830

Cys Leu Gln Glu Thr Leu Cys Ser Thr Val Ser Cys Pro Leu
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 Pro Cys Ala Glu Pro Ile Lys Val Glu Gly Ser Cys Cys Pro Met Cys
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 Pro Glu Met Tyr Val Pro Glu Pro Thr Asn Val Pro Ile Glu Lys Lys
 865 870 875 880
 Asn His Arg Gly Glu Ile Asp Leu Glu Val Pro Met Trp Pro Thr Pro
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 Ser Glu Asn Asp Ile Ile His Leu Pro Arg Asp Met Gly His Leu Gln
 900 905 910
 Val Asp Tyr Arg Asp Asn Asn Arg Leu His Pro Gly Glu Asp Ser Ser
 915 920 925
 Leu Asp Ser Ile Val Ser Val Val Val Pro Ile Ile Ile Cys Leu Ser
 930 935 940
 Ile Ile Ile Ala Phe Leu Leu Ile Asn Gln Lys Lys Gln Trp Val Pro
 945 950 955 960
 Leu Leu Cys Trp Tyr Arg Thr Pro Thr Lys Pro Ser Ser Leu Asn Asn
 965 970 975
 Gln Leu Val Ser Val Asp Cys Lys Lys Gly Thr Arg Val Gln Val Asp
 980 985 990
 Gly Pro Gln Arg Met Leu Arg Ile Ala Glu Pro Asp Ala Arg Phe Ser
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 Tyr Gln Thr Val
 1025

<210> 15
 <211> 2276
 <212> DNA
 <213> Homo sapiens

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 phosphatase catalytic subunit, calcineurin A alpha
 (PPP3CA) cDNA

<220>
 <221> CDS
 <222> (148) .. (1713)
 <223> PPP3CA

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<210> 16
 <211> 521
 <212> PRT
 <213> Homo sapiens

<220>
 <223> human calmodulin-dependent phosphoprotein
 phosphatase catalytic subunit, calcineurin A alpha
 (PPP3CA)

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 Glu Val Phe Asp Asn Asp Gly Lys Pro Arg Val Asp Ile Leu Lys Ala
 35 40 45
 His Leu Met Lys Glu Gly Arg Leu Glu Glu Ser Val Ala Leu Arg Ile
 50 55 60
 Ile Thr Glu Gly Ala Ser Ile Leu Arg Gln Glu Lys Asn Leu Leu Asp
 65 70 75 80

Ile Asp Ala Pro Thr Val Cys Gly Asp Ile His Gly Phe Phe
 35 90 95
 Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro Ala Asn Thr Arg
 100 105 110
 Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr Phe Ser Ile Glu
 115 120 125
 Cys Val Leu Tyr Leu Trp Ala Leu Lys Ile Leu Tyr Pro Lys Thr Leu
 130 135 140
 Phe Leu Leu Arg Gly Asn His Glu Cys Arg His Leu Thr Glu Tyr Phe
 145 150 155 160
 Thr Phe Lys Gln Glu Cys Lys Ile Lys Tyr Ser Glu Arg Val Tyr Asp
 165 170 175
 Ala Cys Met Asp Ala Phe Asp Cys Leu Pro Leu Ala Ala Leu Met Asn
 180 185 190
 Gln Gln Phe Leu Cys Val His Gly Gly Leu Ser Pro Glu Ile Asn Thr
 195 200 205
 Leu Asp Asp Ile Arg Lys Leu Asp Arg Phe Lys Glu Pro Pro Ala Tyr
 210 215 220
 Gly Pro Met Cys Asp Ile Leu Trp Ser Asp Pro Leu Glu Asp Phe Gly
 225 230 235 240
 Asn Glu Lys Thr Gln Glu His Phe Thr His Asn Thr Val Arg Gly Cys
 245 250 255
 Ser Tyr Phe Tyr Ser Tyr Pro Ala Val Cys Glu Phe Leu Gln His Asn
 260 265 270
 Asn Leu Leu Ser Ile Leu Arg Ala His Glu Ala Gln Asp Ala Gly Tyr
 275 280 285
 Arg Met Tyr Arg Lys Ser Gln Thr Thr Gly Phe Pro Ser Leu Ile Thr
 290 295 300
 Ile Phe Ser Ala Pro Asn Tyr Leu Asp Val Tyr Asn Asn Lys Ala Ala
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 Val Leu Lys Tyr Glu Asn Asn Val Met Asn Ile Arg Gln Phe Asn Cys
 325 330 335
 Ser Pro His Pro Tyr Trp Leu Pro Asn Phe Met Asp Val Phe Thr Trp
 340 345 350
 Ser Leu Pro Phe Val Gly Glu Lys Val Thr Glu Met Leu Val Asn Val
 355 360 365
 Leu Asn Ile Cys Ser Asp Asp Glu Leu Gly Ser Glu Glu Asp Gly Phe
 370 375 380
 Asp Gly Ala Thr Ala Ala Ala Arg Lys Glu Val Ile Arg Asn Lys Ile
 385 390 395 400

Arg Ala Ile Glu Lys Met Ala Arg Val Phe Ser Val Leu Glu Glu
 105 410 415

Ser Glu Ser Val Leu Thr Leu Lys Gly Leu Thr Pro Thr Gly Met Leu
 420 425 430

Pro Ser Gly Val Leu Ser Gly Gly Lys Gln Thr Leu Gln Ser Ala Thr
 435 440 445

Val Glu Ala Ile Glu Ala Asp Glu Ala Ile Lys Gly Phe Ser Pro Gln
 450 455 460

His Lys Ile Thr Ser Phe Glu Glu Ala Lys Gly Leu Asp Arg Ile Asn
 465 470 475 480

Glu Arg Met Pro Pro Arg Arg Asp Ala Met Pro Ser Asp Ala Asn Leu
 485 490 495

Asn Ser Ile Asn Lys Ala Leu Thr Ser Glu Thr Asn Gly Thr Asp Ser
 500 505 510

Asn Gly Ser Asn Ser Ser Asn Ile Gln
 515 520

<210> 17

<211> 2194

<212> DNA

<213> Mus musculus

<220>

<223> mouse calmodulin-dependent phosphoprotein
 phosphatase catalytic subunit, calcineurin A alpha
 (PPP3CA) cDNA

<220>

<221> CDS

<222> (76)..(1641)

<223> CTGF

<400> 17

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<210> 18

<211> 521

<212> PRT

<213> Mus musculus

<220>

<223> mouse calmodulin-dependent phosphoprotein
phosphatase catalytic subunit, calcineurin A alpha
(PPP3CA)

<400> 18

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Met Ser Glu Pro Lys Ala Ile Asp Pro Lys Leu Ser Thr Thr Asp Arg
  1             5             10             15

```

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Val Val Lys Ala Val Pro Phe Pro Pro Ser His Arg Leu Thr Ala Lys
      20             25             30

```

```

Glu Val Phe Asp Asn Asp Gly Lys Pro Arg Val Asp Ile Leu Lys Ala
      35             40             45

```

```

His Leu Met Lys Glu Gly Arg Leu Glu Glu Ser Val Ala Leu Arg Ile
      50             55             60

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Ile Thr Glu Gly Ala Ser Ile Leu Arg Gln Glu Lys Asn Leu Leu Asp
      65             70             75             80

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Ile Asp Ala Pro Val Thr Val Cys Gly Asp Ile His Gly Gln Phe Phe
      85             90             95

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Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro Ala Asn Thr Arg
      100            105            110

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Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr Phe Ser Ile Glu
      115            120            125

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Cys Val Leu Tyr Leu Trp Ala Leu Lys Ile Leu Tyr Pro Lys Thr Leu
      130            135            140

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Phe Leu Leu Arg Gly Asn His Glu Cys Arg His Leu Thr Glu Tyr Phe
      145            150            155            160

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Thr Phe Lys Glu Cys Lys Ile Lys Tyr Ser Glu Arg Tyr Asp
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 180 185 190
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 210 215 220
 Gly Pro Met Cys Asp Ile Leu Trp Ser Asp Pro Leu Glu Asp Phe Gly
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 Asn Glu Lys Thr Gln Glu His Phe Thr His Asn Thr Val Arg Gly Cys
 245 250 255
 Ser Tyr Phe Tyr Ser Tyr Pro Ala Val Cys Asp Phe Leu Gln His Asn
 260 265 270
 Asn Leu Leu Ser Ile Leu Arg Ala His Glu Ala Gln Asp Ala Gly Tyr
 275 280 285
 Arg Met Tyr Arg Lys Ser Gln Thr Thr Gly Phe Pro Ser Leu Ile Thr
 290 295 300
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 Val Leu Lys Tyr Glu Asn Asn Val Met Asn Ile Arg Gln Phe Asn Cys
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 Ser Leu Pro Phe Val Gly Glu Lys Val Thr Glu Met Leu Val Asn Val
 355 360 365
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 370 375 380
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 Arg Ala Ile Gly Lys Met Ala Arg Val Phe Ser Val Leu Arg Glu Glu
 405 410 415
 Ser Glu Ser Val Leu Thr Leu Lys Gly Leu Thr Pro Thr Gly Met Leu
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 Pro Ser Gly Val Leu Ser Gly Gly Lys Gln Thr Leu Gln Ser Ala Thr
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 Val Glu Ala Ile Glu Ala Asp Glu Ala Ile Lys Gly Phe Ser Pro Gln
 450 455 460
 His Lys Ile Thr Ser Phe Glu Glu Ala Lys Gly Leu Asp Arg Ile Asn
 465 470 475 480

Glu Arg Met Pro Arg Arg Asp Ala Met Pro Ser Asp Asn Leu
 35 490 495

Asn Ser Ile Asn Lys Ala Leu Ala Ser Glu Thr Asn Gly Thr Asp Ser
 500 505 510

Asn Gly Ser Asn Ser Ser Asn Ile Gln
 515 520

<210> 19
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 <213> Rattus norvegicus

<220>
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 phosphatase catalytic subunit, calcineurin A alpha
 (PPP3CA) cDNA

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 <222> (271)..(1806)
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 (PPP3CA)

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 His Leu Met Lys Glu Gly Arg Leu Glu Glu Ser Val Ala Leu Arg Ile
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 Leu Asp Asp Ile Arg Lys Leu Asp Arg Phe Lys Glu Pro Pro Ala Tyr
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Gly Pro Met Cys Ile Leu Trp Ser Asp Pro Leu Glu Phe Gly
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<223> human protein tyrosine phosphatase, non-receptor
type 3 (PTPN3a) cDNA

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<222> (24) .. (2765)

<223> PTPN3a

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<212> PRT

<213> Homo sapiens

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<223> human protein tyrosine phosphatase, non-receptor
type 3 (PTPN3a)

<400> 22

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```

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Ile His Phe Leu Asp Gly Val Val Gln Thr Phe Lys Val Thr Lys Gln
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Asp Thr Gly Gln Val Leu Leu Asp Met Val His Asn His Leu Gly Val
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Thr Glu Lys Glu Tyr Phe Gly Leu Gln His Asp Asp Asp Ser Val Asp
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```

Ser Pro Arg Trp Leu Glu Ala Ser Lys Pro Ile Arg Lys Gln Leu Lys
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Gly Gly Phe Pro Cys Thr Leu His Phe Arg Val Arg Phe Phe Ile Pro
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Asp Pro Asn Thr Leu Gln Gln Glu Gln Thr Arg His Leu Tyr Phe Leu
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Gln Leu Lys Met Asp Ile Cys Glu Gly Arg Leu Thr Cys Pro Leu Asn
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Ser Ala Val Val Leu Ala Ser Tyr Ala Val Gln Ser His Phe Gly Asp
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Tyr Asn Ser Ser Ile His His Pro Gly Tyr Leu Ser Asp Ser His Phe
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Tyr Cys Asp Lys ████████ Asn Asp Asn Gly Asp Ser Tyr Leu Val ████████ Ile Arg
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Leu Ile Asn Gly Arg Asp Ile Ser Glu His Thr His Asp Gln Val Val
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Met Phe Ile Lys Ala Ser Arg Glu Ser His Ser Arg Glu Leu Ala Leu
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Glu Gly Gly Asp Thr Leu Glu Gly Ser Met Ala Gln Leu Lys Lys Gly
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 660 665 670

Lys Asn Arg Tyr Lys Asp Val Leu Pro Tyr Asp Thr Thr Arg Val Leu
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Leu Gln Gly Asn Glu Asp Tyr Ile Asn Ala Ser Tyr Val Asn Met Glu
 690 695 700

Ile Pro Ala Ala Asn Leu Val Asn Lys Tyr Ile Ala Thr Gln Gly Pro
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Lys Cys His Gln Tyr Trp Pro Asp Pro Pro Asp Val Met Asn His Gly
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Gly Phe His Ile Gln Cys Gln Ser Glu Asp Cys Thr Ile Ala Tyr Val
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Ser Arg Glu Met Leu Val Thr Asn Thr Gln Thr Gly Glu Glu His Thr
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Val Thr His Leu Gln Tyr Val Ala Trp Pro Asp His Gly Ile Pro Asp
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850 855 860

Asn Leu Pro Ile Tyr Pro Leu Asp Ile Val Arg Lys Met Arg Asp Gln
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type 3 (PTPN3) cDNA

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<210> 24

<211> 1028

<212> PRT

<213> Mus musculus

<220>

<223> mouse protein tyrosine phosphatase, non-receptor
type 3 (PTPN3)

<400> 24

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Arg Thr Val Gly Trp Glu Tyr Glu Val Lys Gln Leu Phe Ser Gly Lys
35 40 45

Leu Ala Arg Lys Tyr Ile Pro Asp Ser Ser Asp Ile Phe Ile Glu Lys
50 55 60

Gly Met Val Glu Val Val Gly Tyr Ser Ala Ala Val Met Thr Ser Arg
65 70 75 80

Leu Arg Ala Leu Gly Gly Arg Ile Asn Asn Thr Arg Thr Ser Glu Leu
85 90 95

Pro Lys Glu Lys Thr Arg Ser Glu Val Ile Cys Ser Ile Arg Phe Leu
100 105 110

Asp Gly Leu Val Asn Thr Phe Lys Val Asn Lys Gln Asp Gly Gln
 115 120 125

Ser Leu Leu Asp Met Ala Tyr Gly His Leu Gly Val Thr Glu Lys Glu
 130 135 140

Tyr Phe Gly Leu Gln His Gly Asp Asp Pro Val Asp Ser Pro Arg Trp
 145 150 155 160

Leu Glu Ala Ser Lys Pro Leu Arg Lys Gln Leu Lys Gly Glu Tyr Ala
 165 170 175

Leu Ala Ser Leu Gly Arg Trp Val Tyr Gly Lys Leu Ser Ser Pro Tyr
 180 185 190

Gly Gly Leu Lys Val Ala Gly Lys Pro Asn Leu Phe Leu Lys Asn Val
 195 200 205

Val Gly Gly Phe Pro Cys Thr Leu His Phe Arg Val Arg Tyr Phe Ile
 210 215 220

Pro Asp Pro Asn Thr Leu Gln Gln Glu Gln Thr Arg His Leu Tyr Phe
 225 230 235 240

Leu Gln Leu Lys Met Asp Val Cys Glu Gly Arg Leu Thr Cys Pro Leu
 245 250 255

Asn Ser Ala Val Val Leu Ala Ser Tyr Ala Val Gln Ser His Phe Gly
 260 265 270

Asp Phe Asn Ser Ser Ile His His Pro Gly Tyr Leu Ala Asp Ser Gln
 275 280 285

Phe Ile Pro Asp Gln Asn Asp Asp Phe Leu Ser Lys Val Glu Ser Leu
 290 295 300

His Glu Gln His Ser Gly Leu Lys Gln Ser Glu Ala Glu Ser Cys Tyr
 305 310 315 320

Ile Asn Ile Ala Arg Thr Leu Asp Phe Tyr Gly Val Glu Leu His Gly
 325 330 335

Gly Arg Asp Leu His Asn Leu Asp Leu Met Ile Gly Ile Ala Ser Ala
 340 345 350

Gly Ile Ala Val Tyr Arg Lys Tyr Ile Cys Thr Ser Phe Tyr Pro Trp
 355 360 365

Lys Lys Phe Phe Ile His Gln Arg Gln Lys Gln Glu Glu Lys Ile Val
 370 375 380

Ala Val Arg Ser Ser Asp Pro Val Ala Ile Ser Ala Glu Ser Arg Glu
 385 390 395 400

His Ile Val Ala Phe Asn Met Leu Asn Tyr Arg Ser Cys Lys Asn Leu
 405 410 415

Trp Lys Ser Cys Val Glu His His Ser Phe Phe Gln Ala Lys Lys Leu
 420 425 430

Leu Pro Gln Gl^s Asn Val Leu Ser Gln Tyr Trp Thr Gly Ser
 435 440 445

Arg Asn Pro Lys Lys Ser Val Asn Asn Gln Tyr Cys Lys Lys Val Ile
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Gly Gly Met Val Trp Asn Pro Val Met Arg Arg Ser Leu Ser Val Glu
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Arg Leu Glu Thr Lys Ser Leu Pro Ser Arg Ser Pro Pro Ile Thr Pro
 485 490 495

Asn Trp Arg Ser Pro Arg Leu Arg His Glu Ile Arg Lys Pro Arg His
 500 505 510

Ser Ser Ala Asp Asn Leu Ala Asn Glu Met Thr Tyr Ile Thr Glu Thr
 515 520 525

Glu Asp Val Phe Tyr Thr Tyr Lys Gly Pro Leu Ser Pro Lys Asp Ser
 530 535 540

Asp Ser Glu Val Ser Gln Asn His Ser Pro His Arg Glu Ser Leu Ser
 545 550 555 560

Glu Asn Asn Pro Ala Gln Ser Cys Leu Thr Gln Lys Ser Ser Ser Ser
 565 570 575

Val Ser Pro Ser Ser Asn Ala Pro Gly Ser Cys Ser Pro Asp Gly Val
 580 585 590

Asp Gln Arg Phe Leu Glu Asp Tyr His Lys Val Thr Lys Gly Gly Phe
 595 600 605

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 610 615 620

Gly Tyr Leu Val Leu Ile Arg Ile Thr Pro Asp Glu Glu Gly Arg Phe
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Gly Phe Asn Leu Lys Ala Asp Thr Cys Met Pro Lys Leu Asn Glu Gly
 645 650 655

Asp Gln Ile Val Leu Ile Asn Gly Arg Asp Ile Ser Glu His Thr His
 660 665 670

Asp Gln Val Val Met Phe Ile Lys Ala Ser Arg Glu Ser His Ser Arg
 675 680 685

Glu Leu Ala Leu Val Ile Arg Arg Lys Gly Lys Ala Thr Phe Val Gly
 690 695 700

His Glu Gly Leu Val Pro Ala Arg Ala Val Arg Ser Leu Ala Glu Ile
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Arg Ser Glu Asp Glu Leu Ser Gln Leu Phe Pro Glu Ala Met Phe Pro
 725 730 735

Ala Cys Pro Glu Gly Gly Asp Ser Leu Glu Gly Ser Met Glu Leu Leu
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Lys Lys Gly Leu Ser Gly Thr Val Leu Ile Gln Phe Gln Leu
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 Tyr Arg Lys Lys Pro Gly Leu Ala Val Ser Phe Ala Lys Leu Pro Gln
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 Asn Leu Asp Lys Asn Arg Tyr Lys Asp Val Leu Pro Tyr Asp Thr Thr
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 Arg Val Leu Leu Gln Gly Asn Glu Asp Tyr Ile Asn Ala Ser Tyr Val
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 Asn Met Glu Met Pro Ala Ala Asn Leu Val Asn Lys Tyr Ile Ala Thr
 820 825 830
 Gln Gly Pro Leu Pro Asn Thr Cys Ala Gln Phe Trp Gln Val Val Trp
 835 840 845
 Asp Gln Lys Leu Ser Leu Val Val Met Leu Thr Thr Leu Thr Glu Arg
 850 855 860
 Gly Arg Thr Lys Cys His Gln Tyr Trp Pro Asp Pro Pro Asp Ile Met
 865 870 875 880
 Asp His Gly Ile Phe His Ile Gln Cys Gln Thr Glu Asp Cys Thr Ile
 885 890 895
 Ala Tyr Val Ser Arg Glu Met Leu Val Thr Asn Thr Glu Thr Gly Glu
 900 905 910
 Glu His Thr Val Thr His Leu Gln Tyr Val Ala Trp Pro Asp His Gly
 915 920 925
 Val Pro Asp Asp Ser Ser Asp Phe Leu Glu Phe Val Lys Tyr Val Arg
 930 935 940
 Ser Leu Arg Val Asp Gly Glu Pro Ala Leu Val His Cys Ser Ala Gly
 945 950 955 960
 Ile Gly Arg Thr Gly Val Leu Val Thr Met Glu Thr Ala Met Cys Leu
 965 970 975
 Ile Glu Arg Asn Leu Pro Val Tyr Pro Leu Asp Ile Val Arg Lys Met
 980 985 990
 Arg Asp Gln Arg Ala Met Met Val Gln Thr Ser Ser Gln Tyr Lys Phe
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 Leu Asp Pro Ser
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<210> 25

<211> 2607

<212> DNA

<213> Homo sapiens

<220>

<223> human protein tyrosine phosphatase, non-receptor
type 3 (PTPN3b) splice variant cDNA

<220>

<221> CDS

<222> (1)..(2607)

<223> PTPN3b splice variant

<400> 25

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ttagtccaaa tgctggatcc tagttaa 2607
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<211> 868

<212> PRT

<213> Homo sapiens

<220>

<223> human protein tyrosine phosphatase, non-receptor
type 3 (PTPN3b) splice variant

<400> 26

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35 40 45
Asp Thr Gly Gln Val Leu Leu Asp Met Val His Asn His Leu Gly Val
50 55 60
Thr Glu Lys Glu Tyr Phe Gly Leu Gln His Asp Asp Asp Ser Val Asp
65 70 75 80
Ser Pro Arg Trp Leu Glu Ala Ser Lys Pro Ile Arg Lys Gln Leu Lys
85 90 95
Gly Gly Phe Pro Cys Thr Leu His Phe Arg Val Arg Phe Phe Ile Pro
100 105 110
Asp Pro Asn Thr Leu Gln Gln Glu Gln Thr Arg His Leu Tyr Phe Leu
115 120 125
Gln Leu Lys Met Asp Ile Cys Glu Gly Arg Leu Thr Cys Pro Leu Asn
130 135 140
Ser Ala Val Val Leu Ala Ser Tyr Ala Val Gln Ser His Phe Gly Asp
145 150 155 160
Tyr Asn Ser Ser Ile His His Pro Gly Tyr Leu Ser Asp Ser His Phe
165 170 175
Ile Pro Asp Gln Asn Glu Asp Phe Leu Thr Lys Val Glu Ser Leu His
180 185 190
Glu Gln His Ser Gly Leu Lys Gln Ser Glu Ala Glu Ser Cys Tyr Ile
195 200 205
Asn Ile Ala Arg Thr Leu Asp Phe Tyr Gly Val Glu Leu His Ser Gly
210 215 220
Arg Asp Leu His Asn Leu Asp Leu Met Ile Gly Ile Ala Ser Ala Gly
225 230 235 240
Val Ala Val Tyr Arg Lys Tyr Ile Cys Thr Ser Phe Tyr Pro Trp Val
245 250 255
Asn Ile Leu Lys Ile Ser Phe Lys Arg Lys Lys Phe Phe Ile His Gln
260 265 270
Arg Gln Lys Gln Ala Glu Ser Arg Glu His Ile Val Ala Phe Asn Met
275 280 285
Leu Asn Tyr Arg Ser Cys Lys Asn Leu Trp Lys Ser Cys Val Glu His
290 295 300

His Thr Phe Ph ████ n Ala Lys Lys Leu Leu Pro Gln Glu ████ Asn Val
 305 310 315 320
 Leu Ser Gln Tyr Trp Thr Met Gly Ser Arg Asn Thr Lys Lys Arg Ser
 325 330 335
 Pro Arg Leu Arg His Glu Ile Arg Lys Pro Arg His Ser Ser Ala Asp
 340 345 350
 Asn Leu Ala Asn Glu Met Thr Tyr Ile Thr Glu Thr Glu Asp Val Phe
 355 360 365
 Tyr Thr Tyr Lys Gly Ser Leu Ala Pro Gln Asp Ser Asp Ser Glu Val
 370 375 380
 Ser Gln Asn Arg Ser Pro His Gln Glu Ser Leu Ser Glu Asn Asn Pro
 385 390 395 400
 Ala Gln Ser Tyr Leu Thr Gln Lys Ser Ser Ser Ser Val Ser Pro Ser
 405 410 415
 Ser Asn Ala Pro Gly Ser Cys Ser Pro Asp Gly Val Asp Gln Gln Leu
 420 425 430
 Leu Asp Asp Phe His Arg Val Thr Lys Gly Gly Ser Thr Glu Asp Ala
 435 440 445
 Ser Gln Tyr Tyr Cys Asp Lys Asn Asp Asn Gly Asp Ser Tyr Leu Val
 450 455 460
 Leu Ile Arg Ile Thr Pro Asp Glu Asp Gly Lys Phe Gly Phe Asn Leu
 465 470 475 480
 Lys Gly Gly Val Asp Gln Lys Met Pro Leu Val Val Ser Arg Ile Asn
 485 490 495
 Pro Glu Ser Pro Ala Asp Thr Cys Ile Pro Lys Leu Asn Glu Gly Asp
 500 505 510
 Gln Ile Val Leu Ile Asn Gly Arg Asp Ile Ser Glu His Thr His Asp
 515 520 525
 Gln Val Val Met Phe Ile Lys Ala Ser Arg Glu Ser His Ser Arg Glu
 530 535 540
 Leu Ala Leu Val Ile Arg Arg Arg Ala Val Arg Ser Phe Ala Asp Phe
 545 550 555 560
 Lys Ser Glu Asp Glu Leu Asn Gln Leu Phe Pro Glu Ala Ile Phe Pro
 565 570 575
 Met Cys Pro Glu Gly Gly Asp Thr Leu Glu Gly Ser Met Ala Gln Leu
 580 585 590
 Lys Lys Gly Leu Glu Ser Gly Thr Val Leu Ile Gln Phe Glu Gln Leu
 595 600 605
 Tyr Arg Lys Lys Pro Gly Leu Ala Ile Thr Phe Ala Lys Leu Pro Gln
 610 615 620

Asn Leu Asp Lys Arg Tyr Lys Asp Val Leu Pro Tyr Thr Thr
 625 630 635 640
 Arg Val Leu Leu Gln Gly Asn Glu Asp Tyr Ile Asn Ala Ser Tyr Val
 645 650 655
 Asn Met Glu Ile Pro Ala Ala Asn Leu Val Asn Lys Tyr Ile Ala Thr
 660 665 670
 Gln Gly Pro Leu Pro His Thr Cys Ala Gln Phe Trp Gln Val Val Trp
 675 680 685
 Asp Gln Lys Leu Ser Leu Ile Val Met Leu Thr Thr Leu Thr Glu Arg
 690 695 700
 Gly Arg Thr Lys Cys His Gln Tyr Trp Pro Asp Pro Pro Asp Val Met
 705 710 715 720
 Asn His Gly Gly Phe His Ile Gln Cys Gln Ser Glu Asp Cys Thr Ile
 725 730 735
 Ala Tyr Val Ser Arg Glu Met Leu Val Thr Asn Thr Gln Thr Gly Glu
 740 745 750
 Glu His Thr Val Thr His Leu Gln Tyr Val Ala Trp Pro Asp His Gly
 755 760 765
 Ile Pro Asp Asp Ser Ser Asp Phe Leu Glu Phe Val Asn Tyr Val Arg
 770 775 780
 Ser Leu Arg Val Asp Ser Glu Pro Val Leu Val His Cys Ser Ala Gly
 785 790 795 800
 Ile Gly Arg Thr Gly Val Leu Val Thr Met Glu Thr Ala Met Cys Leu
 805 810 815
 Thr Glu Arg Asn Leu Pro Ile Tyr Pro Leu Asp Ile Val Arg Lys Met
 820 825 830
 Arg Asp Gln Arg Ala Met Met Val Gln Thr Ser Ser Gln Tyr Lys Phe
 835 840 845
 Val Cys Glu Ala Ile Leu Arg Val Tyr Glu Glu Gly Leu Val Gln Met
 850 855 860
 Leu Asp Pro Ser
 865

<210> 27

<211> 861

<212> DNA

<213> Homo sapiens

<220>

<223> human dual specificity phosphatase
 (tyrosine/serine), catalytic domain (DUSP3) cDNA

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 <221> CDS
 <222> (29)..(586)
 <223> DUSP3

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 cgaggtcacc ccgcggatct acgtgggcaa cgcgtctgtg gctcaggaca tccccaagct 180
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<210> 28
 <211> 185
 <212> PRT
 <213> Homo sapiens

<220>
 <223> human dual specificity phosphatase
 (tyrosine/serine), catalytic domain (DUSP3)

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 20 25 30
 Val Thr Pro Arg Ile Tyr Val Gly Asn Ala Ser Val Ala Gln Asp Ile
 35 40 45
 Pro Lys Leu Gln Lys Leu Gly Ile Thr His Val Leu Asn Ala Ala Glu
 50 55 60
 Gly Arg Ser Phe Met His Val Asn Thr Asn Ala Asn Phe Tyr Lys Asp
 65 70 75 80
 Ser Gly Ile Thr Tyr Leu Gly Ile Lys Ala Asn Asp Thr Gln Glu Phe
 85 90 95
 Asn Leu Ser Ala Tyr Phe Glu Arg Ala Ala Asp Phe Ile Asp Gln Ala
 100 105 110
 Leu Ala Gln Lys Asn Gly Arg Val Leu Val His Cys Arg Glu Gly Tyr
 115 120 125
 Ser Arg Ser Pro Thr Leu Val Ile Ala Tyr Leu Met Met Arg Gln Lys
 130 135 140

Met Asp Val Lys Ser Ala Leu Ser Ile Val Arg Gln Asn Glu Ile
 145 150 155 160

Gly Pro Asn Asp Gly Phe Leu Ala Gln Leu Cys Gln Leu Asn Asp Arg
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Leu Ala Lys Glu Gly Lys Leu Lys Pro
 180 185

<210> 29
 <211> 1196
 <212> DNA
 <213> Mus musculus

<220>
 <223> mouse dual specificity phosphatase
 (tyrosine/serine), catalytic domain (DUSP3) cDNA

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 <221> CDS
 <222> (64)..(621)
 <223> DUSP3

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<210> 30
 <211> 185
 <212> PRT
 <213> Mus musculus

<220>
 <223> mouse dual specificity phosphatase
 (tyrosine/serine), catalytic domain (DUSP3)

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25

Val Val Pro Arg Val Tyr Val Gly Asn Ala Ser Val Ala Gln Asp Ile
35 40 45

Thr Gln Leu Gln Lys Leu Gly Ile Thr His Val Leu Asn Ala Ala Glu
50 55 60

Gly Arg Ser Phe Met His Val Asn Thr Ser Ala Ser Phe Tyr Glu Asp
65 70 75 80

Ser Gly Ile Thr Tyr Leu Gly Ile Lys Ala Asn Asp Thr Gln Glu Phe
85 90 95

Asn Leu Ser Ala Tyr Phe Glu Arg Ala Thr Asp Phe Ile Asp Gln Ala
100 105 110

Leu Ala His Lys Asn Gly Arg Val Leu Val His Cys Arg Glu Gly Tyr
115 120 125

Ser Arg Ser Pro Thr Leu Val Ile Ala Tyr Leu Met Met Arg Gln Lys
130 135 140

Met Asp Val Lys Ser Ala Leu Ser Thr Val Arg Gln Asn Arg Glu Ile
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Gly Pro Asn Asp Gly Phe Leu Ala Gln Leu Cys Gln Leu Asn Asp Arg
165 170 175

Leu Ala Lys Glu Gly Lys Val Lys Leu
180 185

<210> 31
<211> 753
<212> DNA
<213> Homo sapiens

<220>
<223> human regulator of G-protein signaling 10 (RGS10)
cDNA

<220>
<221> CDS
<222> (133)..(636)
<223> RGS10

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tggttagcat gtgaagattt taagaaaatg caagataaga cgcagatgca ggaaaaggca 360
aaggagatct acatgacctt tctgtccagc aaggcctcat cacagggtcaa cgtggagggg 420
cagtctcggc tcaacgagaa gatcctggaa gaaccgcacc ctctgatgtt ccagaaactc 480
caggaccaga tctttaatct catgaagtac gacagctaca gccgctttct taagtctgac 540
ttgtttttaa aacacaagcg aaccgaggaa gaggaagaag atttgcctga tgctcaaact 600
gcagctaaaa gagcttcag aatttataac acatgagccc ccaaaaagcc gggactggca 660
gctttaagaa gcaaaggaat ttcctctcag gacgtgccgg gtttatcatt gctttgttat 720

ttgtaaggac tga ggtac aaaacccttc aat

753

<210> 32
<211> 167
<212> PRT
<213> Homo sapiens

<220>
<223> human regulator of G-protein signaling 10 (RGS10)

<400> 32
Met Glu His Ile His Asp Ser Asp Gly Ser Ser Ser Ser Ser His Gln
1 5 10 15
Ser Leu Lys Ser Thr Ala Lys Trp Ala Ala Ser Leu Glu Asn Leu Leu
20 25 30
Glu Asp Pro Glu Gly Val Lys Arg Phe Arg Glu Phe Leu Lys Lys Glu
35 40 45
Phe Ser Glu Glu Asn Val Leu Phe Trp Leu Ala Cys Glu Asp Phe Lys
50 55 60
Lys Met Gln Asp Lys Thr Gln Met Gln Glu Lys Ala Lys Glu Ile Tyr
65 70 75 80
Met Thr Phe Leu Ser Ser Lys Ala Ser Ser Gln Val Asn Val Glu Gly
85 90 95
Gln Ser Arg Leu Asn Glu Lys Ile Leu Glu Glu Pro His Pro Leu Met
100 105 110
Phe Gln Lys Leu Gln Asp Gln Ile Phe Asn Leu Met Lys Tyr Asp Ser
115 120 125
Tyr Ser Arg Phe Leu Lys Ser Asp Leu Phe Leu Lys His Lys Arg Thr
130 135 140
Glu Glu Glu Glu Glu Asp Leu Pro Asp Ala Gln Thr Ala Ala Lys Arg
145 150 155 160
Ala Ser Arg Ile Tyr Asn Thr
165

<210> 33
<211> 877
<212> DNA
<213> Mus musculus

<220>
<223> mouse regulator of G-protein signaling 10 (RGS10)
cDNA

<220>
<221> CDS
<222> (60)..(605)
<223> RGS10

<400> 33
gctcttcggg ctttgcgcc gcgctgccc gctgctccgt cctctggag cccgcggcga 60
tggtcaccgc cgccgtgagc cgactgagca ggaagcggcc gccgtctgat atccatgacg 120
gagatgggag ctcaagcagc ggccaccaga gccttaagag cacagccaag tgggcatacct 180
ccctggagaa tcttctggaa gaccagaag gggtagcag attcagggag tttctgaaga 240
aggaattcag cgaagagaat gtcttggttt ggctagcgtg tgaagatttc aagaaaacgg 300
aggacaggaa gcagatgcag gaaaaggcca aggagatcta catgaccttc ctgtccaata 360
aggcctcttc acaagtcaac gtggaggggc agtctcggct cactgaaaag attctggaag 420
agccacaccc tctgatgttc caaaagctcc aggaccagat cttcaatctc atgaagtatg 480
acagctacag ccgcttcttg aagtctgact tgtttctgaa acccaagcga actgaggaag 540
aggaagaaga gcccccgat gctcagaccg cagctaagcg agcctccaga atttacaaca 600
cataagctga gcccttcacc ccagcgaagg agagggatgg actcttagga ctgtacaggc 660
tgtcatttct ttgttggtgt tgaggactgg agtgtgctag accttccctc tggatatgtg 720
tattttatta actgaacagc aacctctgca tgatgcta atccattaa aaacaaaagt 780
agctttaaag tgfcagttca caaaaacaca tgagattctg ccaatactgg acactcagcc 840
tttcaatcct gattaaagtg ttcgtgaagc tacaagc 877

<210> 34
<211> 181
<212> PRT
<213> Mus musculus

<220>
<223> mouse regulator of G-protein signaling 10 (RGS10)

<400> 34
Met Phe Thr Arg Ala Val Ser Arg Leu Ser Arg Lys Arg Pro Pro Ser
1 5 10 15
Asp Ile His Asp Gly Asp Gly Ser Ser Ser Ser Gly His Gln Ser Leu
20 25 30
Lys Ser Thr Ala Lys Trp Ala Ser Ser Leu Glu Asn Leu Leu Glu Asp
35 40 45
Pro Glu Gly Val Gln Arg Phe Arg Glu Phe Leu Lys Lys Glu Phe Ser
50 55 60
Glu Glu Asn Val Leu Phe Trp Leu Ala Cys Glu Asp Phe Lys Lys Thr
65 70 75 80
Glu Asp Arg Lys Gln Met Gln Glu Lys Ala Lys Glu Ile Tyr Met Thr
85 90 95
Phe Leu Ser Asn Lys Ala Ser Ser Gln Val Asn Val Glu Gly Gln Ser
100 105 110
Arg Leu Thr Glu Lys Ile Leu Glu Glu Pro His Pro Leu Met Phe Gln
115 120 125
Lys Leu Gln Asp Gln Ile Phe Asn Leu Met Lys Tyr Asp Ser Tyr Ser
130 135 140
Arg Phe Leu Lys Ser Asp Leu Phe Leu Lys Pro Lys Arg Thr Glu Glu
145 150 155 160

Glu Glu Glu Gly Pro Asp Ala Gln Thr Ala Ala Lys Ala Ser
 165 170 175

Arg Ile Tyr Asn Thr
 180

<210> 35
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:hexahistidine
 (His) affinity tag

<400> 35
 His His His His His His
 1 5

<210> 36
 <211> 200
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:poly-Gly
 flexible linker

<220>
 <221> MOD_RES
 <222> (6)..(200)
 <223> Gly residues from position 6 to 200 may be present
 or absent

<400> 36
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 1 5 10 15
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 20 25 30
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 35 40 45
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 50 55 60
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 65 70 75 80
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 85 90 95
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 100 105 110
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 115 120 125

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 130 135 140

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 145 150 155 160

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 165 170 175

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
 180 185 190

Gly Gly Gly Gly Gly Gly Gly Gly
 195 200

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